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DEC 07 2006

U.S. Application No.: 10/689,221
AMENDMENT B

Attorney Docket: 3975.025

REMARKS

The foregoing amendments and these remarks are in response to the Office Action dated October 23, 2006. This amendment is timely filed within two months of the mailing of the Final Office Action.

At the time of the Office Action, claims 1-21 were pending. Claims 14-21 have been withdrawn pursuant to an election requirement.

Claim 2 is amended to recite a proper Markush group. No new matter is added.

Claims 1 and 1-5 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting. Applicants submit properly executed terminal disclaimers to overcome these rejections.

Claims 1-13 are rejected under 35 U.S.C. § 103, as being unpatentable over German Patent DE 197 44 809 issued to Berger (hereinafter "Berger"), in view of U.S. Patent No. 4,239,113 issued to Gross *et al.* (hereinafter "Gross") and U.S. Patent No. 3,922,155 issued to Broemer *et al.* (hereinafter "Broemer") and U.S. Patent No. 6,002,065 issued to Constanz *et al.* (hereinafter "Constanz"). Applicants respectfully traverse on the basis of an English translation of relevant portions of Berger.

Reconsideration is requested in view of the following remarks.

Nonstatutory Obviousness-type Double Patenting Rejection

Claim 1 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 of copending Application No. 10/689,219 in view of Gross. Applicants submit a properly executed terminal disclaimer to overcome this rejection.

Claims 1-5 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 7-9, 17 & 21 of copending Application No. 10/689,217 in view of Gross. Applicants submit a properly executed terminal disclaimer to overcome this rejection.

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Claims Rejections – 35 USC § 103

Claims 1-13 are rejected under 35 U.S.C. § 103, as being unpatentable over German Parent DE 197 44 809 issued to Berger (hereinafter "Berger"), in view of U.S. Patent No. 4,239,113 issued to Gross *et al.* (hereinafter "Gross") and U.S. Patent No. 3,922,155 issued to Broemer *et al.* (hereinafter "Broemer") and U.S. Patent No. 6,002,065 issued to Constanz *et al.* (hereinafter "Constanz"). Reconsideration is requested in view of the following remarks.

The position of the Examiner can be found on pages 3-8 of the Office Action. Of particular importance, the Examiner asserts that claim 7 of Burger reads directly upon instant claim 7. The Examiner states that:

The abstract of DE 197 44 809 C1 discloses a porous rapidly soluble glass ceramic comprising $\text{Ca}_2\text{KNa}(\text{PO}_4)_2$, $\text{Ca}_5\text{Na}_2(\text{PO}_4)_2$ or $\text{Ca}_6\text{Na}_3(\text{PO}_4)_5$ as the main crystal phase which is useful as a resorbable bone substitute, a substrate for drugs (e.g. antibiotics), proteins, enzymes or cells or a filter aid. Claim 7 of DE 197 44 809 C1 clearly claims a composition comprising (wt %):

30-50	P_2O_5
20-55	CaO
5-25	Na_2O
0.01-20	K_2O
0-15	MgO
0-10	SiO_2

The composition reads upon instant claim 7. It is the Examiner's position that heat melting these material will intrinsically form the instantly claimed phosphate mixtures in instant claim 1 including an amorphous phase, which makes up 0.1 to 65% by weight and 0.1-15% by weight chain phosphates. In addition, since magnesium is present in the composition, then it is reasonable to assert that mixed crystals would intrinsically form in the ceramic material.

Office Action page 3.

Applicants respectfully traverse in light of the attached English language translation of the relevant portion of Burger.

Before reviewing the cited art, Applicants wish to review the claimed invention in detail. The invention, as set forth in claim 1, is drawn to a powder mixture for a resorbable calcium phosphate biocement. The biocement particles consist of 40-99 %-vol of particles with a particle size of 0.1-10 micrometers, 1-20 %-vol of particles with a particle size of 10-43 micrometers,

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and 0-59% of particles with a particle size of 43-315 micrometers. The material comprising the particles has several important features (outline headings included for ease of discussion below):

1) The material is a product-by-process produced by the process of:

- a) Homogenizing and drying a mixture of 30-55% by weight CaO, 35-50% by weight P₂O₅, 1-20% by weight Na₂O, 0.5-20% by weight K₂O and 0.1-5% by weight MgO and optionally up to 5% by weight SiO₂,
- b) Subjecting the mixture to a step-by-step thermal treatment lasting 1-2h at each of 350-450°C, 750-850°C and 950-1,050°C, respectively,
- c) Continuing to heat the mixture to melt the mixture at between 1,550 and 1,650°C, holding the mixture at the melting temperature for between 10 and 60 minutes,
- d) Cooling the mixture in a spontaneous or temperature-controlled manner, and
- e) Grinding it to the appropriate particle sizes (0.1-10 micrometers, 10-43 micrometers & 43-315 micrometers).

2) After the process in step 1), above, the phosphorous content of the particulate material comprises:

- a) 65-99.9 %-wt of orthophosphates,
- b) 0.1-35 %-wt of diphosphate, and
- c) in claim 2, 0.1 – 15%-wt of chain phosphates

3) After the process in step 1), above, the particulate material comprises 35-99.9 %-wt of a main crystal phase, 0.1-20 %-wt of a secondary crystal phase, and 0.1-65%-wt of an x-ray amorphous phase.

- a) The main crystal phase is selected from the group consisting of Ca₂K_{1-x}Na_{1+x}(PO₄)₂, where x = 0.1 to 0.9, Ca₁₀Na(PO₄)₇, Ca₁₀K(PO₄)₇, mixtures thereof and mixed crystals according to the general formula Ca₁₀K_xNa_{1-x}(PO₄)₇, where x = 0 to 1.
- b) The secondary crystal phase is selected from the group consisting of

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$\text{Na}_2\text{CaP}_2\text{O}_7$, $\text{K}_2\text{CaP}_2\text{O}_7$, $\text{Ca}_2\text{P}_2\text{O}_7$, NaPO_3 , KPO_3 and mixtures thereof.

c) The composition of the x-ray amorphous phase is not defined in claim 1, however, it is some combination of the compounds used to form the powder material.

An important aspect of the claimed invention is the percentage of orthophosphates, diphosphates and, in claim 2, chain phosphates. Another important aspect of the claimed invention is the percentage of a main crystal phase, a second crystal phase and an amorphous phase. Another important aspect of the claimed invention is the limited number of species of which the crystal phases may consist (claimed using a Markush group), which includes mixed crystals having a specific formula $(\text{Ca}_{10}\text{K}_x\text{Na}_{1-x})(\text{PO}_4)_7$, where $x = 0$ to 1).

In order to clarify the content of Berger, Mr. Wolf-Jürgen Walter, a German Patent Attorney, has provided a sworn translation of a portion of Berger, page 2, line 22 to page 3, line 10, see Attached Translation and oath dated December 4, 2006. Mr. Wolf indicates that the translated portion of Berger describes the content of claim 7 of the Berger.

Referring to the translation, claim 7 of Berger is drawn to a molded article manufactured by melting together 40-70 %-wt of a prepared glass ceramic, having the weight percentages of CaO , P_2O_5 , Na_2O , K_2O , MgO and SiO_2 cited by the Examiner, and 30-60 %-wt of a borosilicate glass. This glass ceramic and borosilicate glass mixture is melted together by heating the materials to 1450°C . The two material mixture is held at 1450°C for a period of less than 2 hours, see *Translation*, page 2. During cooling of the two material mixture the temperature is held at $400\text{--}450^\circ\text{C}$ for 15 to 120 minutes, see *Translation*, middle of p. 1. After the material has cooled, an alkaline solvent is used to remove the majority of the borosilicate phase.

A comparison of Berger and the claimed invention should help clarify the distinctions between Berger and the claimed invention. In order to anticipate, or render the claimed invention obvious, Berger must disclose or suggest both the desirability of the claimed composition and a method of creating the claimed composition. After reviewing the translation

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of Berger, it is clear that Berger simply does not meet this standard.

In Berger, the prepared glass ceramic, having a chemical synthesis composition of CaO , P_2O_5 , Na_2O , K_2O , MgO and SiO_2 , is a raw material comprising 40-70% of a two component system. Berger does not disclose anything about the crystal phases or the phosphates in the glass ceramic raw material. The only information we have with respect to the crystal phases or the phosphates of Berger is that after being mixed with a borosilicate glass, exposed to a thermal treatment, and leached with a alkali solvent, there is a main crystal phase of $\text{Ca}_2\text{KNa}(\text{PO}_4)_2$, $\text{Ca}_3\text{Na}_2(\text{PO}_4)_2$, or $\text{Ca}_6\text{Na}_3(\text{PO}_4)_5$.

Applicants previously pointed out that Berger does not disclose or suggest the claimed invention because Berger contains only crystals of $\text{Ca}_2\text{KNa}(\text{PO}_4)_2$, $\text{Ca}_3\text{Na}_2(\text{PO}_4)_2$, or $\text{Ca}_6\text{Na}_3(\text{PO}_4)_5$. In response to this remark made in Amendment A filed July 10, 2006, the Examiner states that "the comprising language of the instant claim 1 does not preclude the presence of the crystals disclosed by Berger," *see Office Action*, page 7. Applicants refer the Examiner to outline features 3)a) and 3)b), set forth above, of the claimed invention. As set forth in these features, the main crystals and secondary crystals of the claimed invention are limited to enumerated members of a Markush group. A comparison clearly shows that the Markush group of the claimed invention do not include the crystals described in Berger: $\text{Ca}_2\text{KNa}(\text{PO}_4)_2$, $\text{Ca}_3\text{Na}_2(\text{PO}_4)_2$, and $\text{Ca}_6\text{Na}_3(\text{PO}_4)_5$. Clearly, no "comprising language" is present in the relevant portions of the claimed invention. Accordingly, Berger does not disclose or suggest the claimed invention.

It is well know in the art that the type of crystalline phases and amorphous phases and the relative percentages of each are directly linked to the melting and cooling process, in particular tempering steps, to which the starting material is exposed. Similarly, it is well known that the inorganic compounds formed during a heating process is directly linked to the hold points and maximum temperature reached during the heating process. Instant claim 1 is a product-by-process claim reciting specific conditions for preparing the claimed powder mixture. *These conditions are the only method know to the inventors to achieve the mixture of crystalline and*

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amorphous phases with the claimed mixture of orthophosphates, diphosphates, and, as in claim 2, chain phosphates.

The clearly distinguishable crystal compositions in Berger and the present invention results because of their divergent thermal history. This divergent thermal history is clearly set forth for ease of comparison in rows 3, 4 & 5 of Comparison Table 1, below, and the following summary:

- The claimed invention includes three holds (350-450°C, 750-850°C and 950-1,050°C) during the heating process, Berger discloses none.
- The claimed invention has a maximum heating temperature of 1550-1650°C, whereas Berger's maximum heating temperature is 1400-1520°C.
- The claimed invention allows spontaneous cooling or temperature-controlled cooling without any holding step, whereas Berger includes a holding step in the range of 400-450°C.

Even without a translation, a review of the Berger document confirms the divergent thermal history. The three holding temperature ranges of the claimed invention are simply not disclosed or suggested by Berger. Furthermore, the different compounds of the crystal structures is evidence that Berger does not even rely on the claimed material as a raw material. In fact, the only temperatures anywhere in the Berger document are:

- (i) the range of 70 to (bis) 98°C (for example, p. 5, ln 38)
- (ii) 80°C (for example, Berger, p. 3, ln. 6 & p. 4, ln. 28)
- (iii) the range of 450 to 400°C (for example, Berger, p. 3, ln. 44 & p. 4, ln. 23)
- (ii) 1450°C (for example, Berger p. 3, ln. 3 & p. 4, ln. 19)

Clearly, Berger does not disclose or suggest the thermal treatment required to form the claimed invention. Because of these divergent thermal treatments, the glass ceramic from Berger and the material of the claimed invention contain different amounts of crystalline and amorphous phases and crystals with different chemical compositions. Clearly, Berger does not disclose or suggest a material with the claimed main crystal phase or the claimed secondary crystal phase,

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both of which are limited to enumerated members of Markush groups. Accordingly, Applicants believe that claim 1 and all claims dependent thereon are drawn to patentable subject matter.

Comparison Table 1 – Comparing the process used in Berger (DE 197 44 809) to that of instant claim 1.

Process	
U.S. Serial No. 10/689,221	Berger (DE 197 44 809)
1. Melting together a powder mixture of CaO, P ₂ O ₅ , Na ₂ O, K ₂ O & MgO	1. Melting together two separate substances: a) a phosphate containing glass ceramic having a chemical synthesis composition of CaO, P ₂ O ₅ , Na ₂ O, K ₂ O & MgO & b) a borosilicate glass
2. No Boron	2. Contains 0.05-2% boron by weight (see claim 1)
3. Tempering holds during heating at: a) 350-450°C b) 750-850°C c) 950-1050°C	3. No tempering holds during heating
4. Melting temperature of 1550-1650°C	4. Melting temperature of 1400-1520°C (see claim 8)
5. No holds. Spontaneous cooling or temperature-controlled cooling	5. Holding step at 400-450°C during cooling
6. Ground.	6. Extraction of borosilicate phase using an alkaline solution
PRODUCT: Powder mixture of crystal phases and x-ray amorphous (non-crystal) phases	PRODUCT: A glassy-crystal body.

The Examiner also asserts that "since magnesium is present in the composition, then it is reasonable to assert that mixed crystals would intrinsically form in the ceramic material," *see Office Action*, p. 3 last line, p. 4 first two lines. As indicated in 3)a) of the outline of claim 1 above, the main crystal phase is selected from the group consisting of Ca₂K_{1-x}Na_{1+x}(PO₄)₂, where x = 0.1 to 0.9, Ca₁₀Na(PO₄)₇, Ca₁₀K(PO₄)₇, mixtures thereof and *mixed crystals according to the general formula* Ca₁₀K_xNa_{1-x}(PO₄)₇, *where x = 0 to 1*. Applicants point out that the Examiner's assertion cannot be correct because the composition of the mixed crystals is limited to a general formula that does not contain magnesium and the main crystal phase is limited to a

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Markush group, of which the mixed crystals are an enumerated element.

As set forth above, the product prepared by present claim 1 differs from Berger in that it contains different phases (crystalline and amorphous), different chemical compounds (phosphates, diphosphates, chain phosphates & mixed crystals), different chemical elements (no boron in the present claims), and even different physical properties. Clearly, Berger does not disclose all elements of the claimed invention. Accordingly, Applicants believe that claim 1 and all claims dependent thereon are drawn to allowable subject matter.

Applicants further traverse the opinion of the Examiner that claims 1-13 are unpatentable over Gross, Broemer, and Constantz.

As indicated by the Examiner, Gross is a bone cement wherein the bioactive glass ceramic powder has a particle size of 10-200 micrometers. Gross teaches toward the middle of that range, with a narrow preferred range limited to between 90 and 125 micrometers, *see Gross*, col. 2, ln. 26-28. In contrast, the claimed invention claims a particle distribution with 40-99% powder with a diameter between 0.1 and 10 micrometers, 1-20% powder with a diameter between 10 and 43 micrometers, and 0-59% powder with a diameter between 43 and 315 micrometers. Thus, Gross teaches away from using particles that comprise 40 to 99% of the particles in the claimed invention. Clearly, one of ordinary skill in the art would not have been motivated to prepare a mixture with 40-99% particles outside the broad range disclosed by Gross, especially because the preferred range taught by Gross is, at a minimum, 10 times larger than the claimed range. Accordingly, Applicants believe that claim 1 and all claims dependent thereon are directed to patentable subject matter.

The Court of Appeals stated that for combination inventions: "Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. Under section 103, teachings of references can be combined only if there is some suggestion or incentive to do so ..."

The rejection as it pertains to Broemer refers to the addition of calcium orthophosphate $\text{Ca}_3(\text{PO}_4)_2$ to a mixture of SiO_2 , NaO_2 , KO_2 and MgO_2 and melting down that mixture and

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cooling the melt with a special temperature-time ceramization program. In the present invention the X-ray diffractometric measurements in claim 1 show no $\text{Ca}_3(\text{PO}_4)_2$, but only $\text{Ca}_2\text{K}_{1-x}\text{Na}_{1+x}(\text{PO}_4)_2$, where $x = 0.1$ to 0.9 , $\text{Ca}_{10}\text{Na}(\text{PO}_4)_7$ and $\text{Ca}_{10}\text{K}(\text{PO}_4)_7$ as the orthophosphates.

Claim 9 of the pending claim refers to the possible addition of a $\text{Ca}_3(\text{PO}_4)_2$ powder to the other powder made using the melting and grinding steps. Broemer discloses that $\text{Ca}_3(\text{PO}_4)_2$ may be added to the mixture of raw materials prior to melting; however, the present invention adds a separate $\text{Ca}_3(\text{PO}_4)_2$ powder to the powder already formed by the process in claim 1. Clearly, the teaching of Broemer combined with Berger would lead one to add $\text{Ca}_3(\text{PO}_4)_2$ prior to the melting process, not as a separate powder, as in the claimed invention. Accordingly, there would be no motivation to combine Broemer with Berger in a manner that would lead to the claimed invention. Accordingly, Applicants believe that claim 1 and all claims dependent thereon, including claim 9, are drawn to allowable subject matter.

Constantz et al teaches kit for preparing a calcium phosphate cement composition which is a calcium phosphate mineral – see claim 1 col. 11 line 11. Such a mineral is a solid and not biological resorbable because that would be in contrast to its function: "to introduce relatively long lived structures into the body to provide the necessary stability and support required for fillers, prosthetic devices and the like" (col. 10 line 63-67).

For at least the above reasons Applicants believe independent claim 1 and all claims dependent thereon are drawn to allowable subject matter.

The Commissioner is hereby authorized to charge the \$130.00 fee for two terminal disclaimers to Deposit Account No. 50-0951. No additional fees are believed due; however, the Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, to Deposit Account No. 50-0951.

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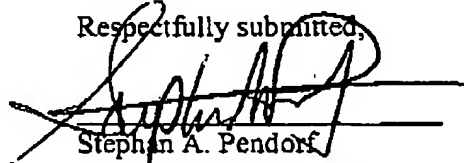
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Favorable consideration and early issuance of the Notice of Allowance are respectfully requested. Should further issues remain prior to allowance, the Examiner is respectfully requested to contact the undersigned at the indicated telephone number.

Date: December 7, 2006

Respectfully submitted,



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Translation of DE 197 44 809 C1, page 2 line 22 to page 3 line 10

The subject-matter of the invention is a porous, vitreous-crystalline moulded article with a quick solubility and with the calcium phosphate main crystal phases $\text{Ca}_2\text{KNa}(\text{PO}_4)_2$, $\text{Ca}_3\text{Na}_2(\text{PO}_4)_2$ or $\text{Ca}_4\text{Na}_3(\text{PO}_4)_5$, characterised by the following features:

- the boron content is in the range of 0.05 to 2 percent by weight
- the moulded article has open pores with an overall porosity of 33 to 80 %,
- the diameter of the pores is 0.2 to 50 μm
- the solubility under simulated physiological conditions in 0.2 M TRIS-HCl-buffer solution at 37° C and a pH value of 7.1 to 7.5 is 300 to 4000 mg/litre solvent/day,
- the moulded article is chemically stable at a pH value within the range of greater than 8,
- the surface of the porous moulded article is within the range of 1 to 40 m^2/g (according to BET).

The above-mentioned moulded article is manufactured by melting together within less than 2 hours two separately prepared glasses or glass ceramics, one material consisting of 70 to 40 percent by weight of a calcium-phosphate-containing vitreous-crystalline material (glass ceramic) which corresponds to the chemical synthesis composition (data in percent by weight):

20-55 CaO , 5-25 Na_2O , 0.01-20 K_2O , 0-15 MgO , 30-50 P_2O_5 , 0-15 SiO_2 ,

and the other material consisting of 30 to 60 percent by weight of a borosilicate glass which corresponds to the chemical synthesis composition (data in percent by weight)

15-55 B_2O_3 , 0-15 Na_2O , 0-15 K_2O , 30-75 SiO_2 ,

and the melt, after having been cooled down to a temperature within the range of 450 to 400° C, at which it is kept for 15 to 120 minutes, the melt is subsequently cooled down further to ambient temperature and subjected to a leaching by means of an alkaline solvent in order to remove almost completely the borosilicate phase until a moulded article with open pores is obtained so that a material with open pores and with the synthesis composition of the calcium-phosphate-containing vitreous-crystalline material is obtained with a main crystal phase depending upon the used borosilicate glass.

A preferred glass ceramic consists of (in percent by weight)

25-35 CaO , 5-15 Na_2O , 13-18 K_2O , 1-5 MgO , 35-45 P_2O_5 , 0-3 SiO_2 .

A preferred glass consists of 15-30 B_2O_3 , 0-15 Na_2O , 0-15 K_2O , 60-75 SiO_2 .

With this combination of actually known absorbable glass-ceramic bone substitute materials

and actually known borosilicate glasses, it is possible - when adhering to the process steps which are described above and mentioned below - to obtain materials which absorb quickly in an acid and a neutral medium and which in addition show an open porosity. The surprising feature of this combination is that contrary to all expectations no mixing of the individual components, i.e. of the calcium-phosphate glass ceramic and of the borosilicate glass occurs when the process parameters which are described further are adhered to.

When immiscibilities are observed at all between individual glasses, these are then, as a general rule, droplet-like segregations. This would mean that in a matrix (for example calcium-phosphate-containing glass-ceramic component) droplet-like structures are dispersed (for instance borosilicate glass component). This surprising finding, i.e. that a so-called spinodal segregation with a mutual penetration structure may occur when the process conditions which are further described below are adhered to, was not to be expected even by the specialised glass expert.

This penetration structure now makes it possible that the moulded article which is obtained by means of the melt of the two components at about 1450° C and a melting period of maximally 2 hours, preferably maximally 30 minutes, in particular 5 to 15 minutes can be extracted, before or after granulation into corresponding fractions as required by the application, in a further process step by means of alkaline solution, for instance 2.5 N NaOH at 80° C so that the component that is soluble in alkaline solution, the borosilicate glass separates and the desired moulded article with open pores which consists of the quickly absorbable glass-ceramic material remains as residue. The said material is quickly soluble under physiological conditions (pH = 7.4) and under acid conditions, but is chemically very stable under alkaline conditions, i.e. at a pH of > 8 which must be taken into account in respect of its possible use as a filter material.

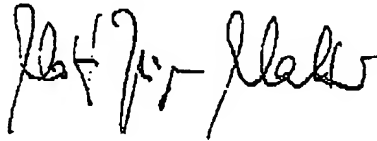
I, Wolf-Jürgen Walter,

of, Schirnerstrasse 37, D-12524 Berlin, Germany

do hereby certify that I am well acquainted with the English and German languages and that the attached is a true translation into the English language of

DE 197 44 809 C1 page 2 line 22 to page 3 line 10

Signature

A handwritten signature in black ink, appearing to read 'Wolf-Jürgen Walter', written in a cursive style.

Dated this 4th day of December 2006